AUSTRALIAN PRODUCT INFORMATION – MINIMS® PILOCARPINE NITRATE (PILOCARPINE NITRATE) EYE DROPS

1 NAME OF THE MEDICINE

Pilocarpine Nitrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Minims Pilocarpine Nitrate Eye Drops contains pilocarpine nitrate 2% (20 mg/mL). No preservatives are included in the formulation.

For the full list of excipients, see section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

A single-use eye drops, solution.

Minims Pilocarpine Nitrate Eye Drops are single-use, clear, colourless sterile ophthalmic solutions. No preservatives are included in the formulation.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Chronic glaucoma and a miotic for reversing the effects of the weaker mydriatics and in emergency treatment of glaucoma.

4.2 DOSE AND METHOD OF ADMINISTRATION

For topical ophthalmic use only. Not for injection into the eye

Miotics are normally administered at the end of an ophthalmological examination while mydriatics are given at the beginning.

Systemic absorption may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following instillation of drops. It is especially advisable when administering pilocarpine to children.

Adults (including the elderly) and children

Miosis: To induce miosis 1 or 2 drops should be used.

Glaucoma: In cases of emergency treatment of acute narrow angle glaucoma, 1 drop should be used every 5 minutes until miosis is achieved.

Each Minims unit should be discharged after a single use.

4.3 CONTRAINDICATIONS

Miotics are contraindicated in conditions where pupillary constriction is undesirable such as acute iritis, pupillary block glaucoma, acute uveitis, anterior uveitis, iridocyclitis, acute iritis and some forms of secondary glaucoma.

Hypersensitivity to pilocarpine nitrate.

Retinal detachment; past history of retinal detachment or conditions that predispose to retinal detachment.

Use of soft contact lenses when administering pilocarpine eye drops (see section 4.4 Special Warnings and Precautions for Use).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Administration

For topical ophthalmic use only. Not for injection into the eye.

Systemic absorption

Systemic reactions rarely occur when treating chronic simple glaucoma at normal doses. However, in the treatment of acute closed angle glaucoma the possibility of systemic reactions must be considered because of the higher doses given (more frequent administration).

Systemic absorption in adults may be reduced by nasolacrimal occlusion or closing the eyelids for 2 minutes after the instillation of the drops (this blocks the passage of the drops via the nasolacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa).

In pediatric patients lacrimal punctum should be occluded for one minute with a finger to limit systemic exposure.

Pilocarpine ophthalmic solution should be used with caution on an inflamed eye as hyperaemia greatly increases the rate of systemic absorption through the conjunctiva. Caution is particularly advised in patients with acute heart failure, bradycardia, coronary artery disease, bronchial asthma and other chronic respiratory diseases, peptic ulceration, hypertension, urinary tract obstruction, Parkinson's disease and corneal abrasions.

Primary Congenital Glaucoma

Caution is advised when using pilocarpine ophthalmic solution in pediatric patients with primary congenital glaucoma for control of intraocular pressure (IOP) as cases of paradoxical increase in IOP have been reported.

Pre-existing retinal disease

Retinal detachments have been caused in susceptible individuals and those with pre-existing retinal disease; therefore, fundus examination is advised in all patients prior to the initiation of therapy.

Poor illumination

Miosis causes difficulty in dark adaptation. Caution is therefore necessary when driving at night or performing hazardous tasks in poor illumination. (See section 4.8. Adverse Effects (Undesirable Effects)).

Long-term treatment

Patients with chronic glaucoma on long-term pilocarpine therapy should have regular monitoring of intraocular pressure and visual fields.

If possible, treatment with long-acting miotics should be discontinued before surgery on the eye as there is an increased risk of hyphaemia.

Pilocarpine induces spasm of the ciliate muscle which may last up to two hours. Topical miotics may precipitate bronchospasm in susceptible patients.

Use of soft contact lenses

Miotics should not be used by patients wearing soft contact lenses.

Use in the elderly

No data available

Paediatric use

No data available

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Belladonna alkaloids or cyclopentolate used ophthalmically may interfere with the miotic effects of pilocarpine and may have their own mydriatic effects reduced. This latter effect may be used to therapeutic advantage.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available

Use in pregnancy – Pregnancy Category B3

Safety for use in pregnancy has not been established, therefore, use only when considered essential by the physician.

Use in lactation

Safety for use in lactation has not been established, therefore, use only when considered essential by the physician.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Pilocarpine may cause transient blurring of vision on instillation. Patients should be warned not to drive or operate hazardous machinery unless vision is clear.

Pilocarpine may also cause difficulty with dark adaptation and caution is necessary with driving or performing hazardous tasks in poor illumination.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

Following ocular administration pilocarpine is usually better tolerated than the anticholinesterases but in common with other miotics may produce ciliary spasm, ocular pain and irritation, blurred vision, lachrymation, myopia, and browache.
Conjunctival vascular block has been reported. Lens opacities have occurred following prolonged use. Treatment with miotics should be stopped if symptoms of systemic toxicity develop.

Systemic adverse effects after the ophthalmic use of pilocarpine are thought to be rare and reports of toxicity appear to involve elderly patients treated for acute angle-closure glaucoma prior to surgery and who received 2 to 5 times the usual daily dose of pilocarpine in a few hours.

Adverse effects reported are listed in the CIOMS table below. These are listed by system organ class and frequency categories: Very common (≥10%), Common (≥1% to <10%), uncommon (≥0.1% to <1%), rare (≥0.01% to <0.1%), very rare (<0.01%), not known (cannot be estimated from available data).

System Organ Class	Frequency	CCDS Term	MedDRA PT v20.0
Nervous system disorders	Not known	Browache Headache	Headache
Eye disorders	Not known	Ciliary muscle spasm *correlated term:* Accommodation spasm	Ciliary muscle spasm
		Conjunctival hyperaemia *correlated term:* Conjunctival vascular congestion	Conjunctival hyperaemia
		Eye irritation *correlated term:* Burning, Eye itching	Eye irritation
			Eye pruritus
		Eye pain	Eye pain
		Eyelid pain *correlated term:* Muscle cramps of the eyelid	Eyelid pain
		Increased – pupillary block	Pupillary block
		Iris adhesions	Iris adhesions

		Keratitis	Keratitis
		Lacrimation increased	Lacrimation increased
		Lens changes (lens dislocation, lens opacity) with prolonged use	Lens dislocation
			Lens opacity
		Myopia transient *correlated term:* Pseudomyopia (fluctuating vision)	Myopia
			Pseudomyopia
		Retinal detachment	Retinal detachment
		Visual acuity reduced in poor illumination *correlated term:* Poor night vision Blurred vision	Visual acuity reduced
			Night blindness
			Vision blurred
		Vitreous haemorrhage	Vitreous haemorrhage
Cardiac disorders	Not known	Bradycardia	Bradycardia
		Changes in cardiac rhythm	Arrhythmia
		Pulmonary oedema	Pulmonary
Vascular disorders	Not known	Hypotension	Hypotension
Respiratory, thoracic, and mediastinal disorders	Not known	Bronchospasm	Bronchospasm
		Pulmonary oedema	Pulmonary oedema
Gastrointestinal disorders	Not known	Abdominal spasm	Abdominal rigidity
		Diarrhoea	Diarrhoea
		Nausea	Nausea
		Salivary hypersecretion	Salivary hypersecretion
		Tenesmus	Rectal tenesmus
		Vomiting	Vomiting
General disorders and administration site conditions	Not known	Hyperhidrosis	Hyperhidrosis

4.9 OVERDOSE

Should accidental overdosage in the eye(s) occur, flush eye(s) with water or normal saline. If accidentally ingested, induce emesis or perform gastric lavage. Observe patients for signs of pilocarpine toxicity ie. salivation, lacrimation, sweating, nausea, vomiting and diarrhoea. If these occur, therapy with anticholinergics (atropine) may be necessary. Bronchial constriction may occur in asthmatic patients.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Pilocarpine is a miotic: its action commences a few minutes after instillation and continues for about six hours. Although not as active as physostigmine, it does have the important advantage that there is an absence of pain and the miotic action is of shorter duration.

Pilocarpine is a tertiary amine direct-acting parasympathomimetic agent with primarily the muscarinic effects of acetylcholine. It is mainly used as a miotic in the treatment of glaucoma and in ophthalmological procedures.

It is much better pharmacologically to reverse mydriasis by using a drug that acts on the same muscle as the mydriatic. If an antimuscarinic has been used which paralyses the sphincter pupillae muscle, then ideally pilocarpine should be used. Pilocarpine is adequate only against the weaker mydriatics such as tropicamide and phenylephrine.

Miotics should return the size of the pupil to normal, have a length of action of the same order but slightly longer than the mydriatic and not cause any local or systemic toxicity.

Pilocarpine acts directly on the muscarinic receptors on the smooth muscle of the sphincter pupillae and its action is independent of a functioning sympathetic nerve supply. Following the use of eye drops, miosis occurs in 10 to 30 minutes and lasts 4 to 8 hours while peak reduction in intra-ocular pressure occurs in 75 minutes and the reduction usually lasts for 4 to 14 hours.

Glaucoma: Pilocarpine may be used when miotics are required to reduce intra-ocular pressure in the treatment of open–angle glaucoma and is commonly administered with topical beta-blockers or adrenergic agents. Chronic open-angle glaucoma is the commonest form and is due to blockage in drainage through the trabecular meshwork. Intra-ocular pressure increases gradually, and the condition is usually asymptomatic until well advanced and severe damage has occurred. Usually both eyes are affected. Risk factors include old age, diabetes, a family history and myopia.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Absorption

No data available

Distribution

No data available

Metabolism

No data available

Excretion

No data available

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available

Carcinogenicity

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Purified Water

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C to 8°C. (Refrigerate. Do not freeze.) Do not expose to strong light.

6.5 NATURE AND CONTENTS OF CONTAINER

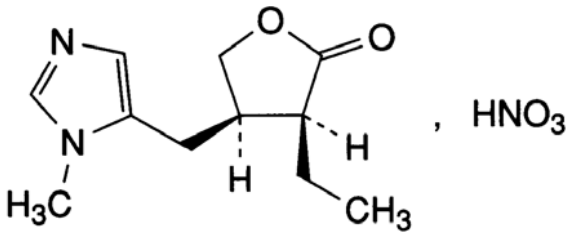
Minims Pilocarpine Eye Drops are supplied in a single use polypropylene tube (unit) overwrapped in a polyester/paper blister. The blisters are packed in cartons of 20 units. Each unit contains approximately 0.5 mL solution.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



Chemical name: (3S,4R)-3-ethyl-4-[(1-methyl-1H-imidazol-5-yl)methyl]-dihydro- 3H- furan-2-one nitrate.

Molecular formula: $C_{11}H_{16}N_2O_2HNO_3$

Molecular weight: 271.3

Pilocarpine Nitrate is a white crystalline powder or colourless crystals, sensitive to light, freely soluble in water, sparingly soluble in alcohol, practically insoluble in ether. It melts at about 174°C with decomposition.

CAS number

CAS number: 148-72-1

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 - Prescription Only Medicine

8 SPONSOR

Bausch & Lomb (Australia) Pty Ltd
Level 2, 12 Help Street
Chatswood, NSW 2067

9 DATE OF FIRST APPROVAL

4 August 1999

10 DATE OF REVISION

4 January 2019

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	New PI format
Contraindications	Update as per CCDS-025/Rev.01, 30. August 2017
Special Warnings and Precautions	Update as per CCDS-025/Rev.01, 30. August 2017
Adverse Effects	Update as per CCDS-025/Rev.01, 30. August 2017